Richard Winfield Hanson (1936–2014)

Richard W. Hanson, the Leonard and Jean Skeggs Professor of Biochemistry and Distinguished University Professor at Case Western Reserve School of Medicine, died on February 28, 2014, after a 20 year battle with cancer. A brilliant scientist, award-winning teacher, and devoted university citizen, Hanson was the quintessential "complete package." He was known to his friends and colleagues as the "maestro of metabolism"—a scientist who displayed a lifelong understanding of and appreciation for the beauty and complexity of intermediary metabolism. His enthusiasm for science in general and his chosen field in particular was infectious, and for those of us who were privileged to study with him, he was a mentor *par excellence.* Most importantly, he was a warm, compassionate, and modest man, whose dimples were permanently etched into his face because smiling was his natural state.

Richard Hanson grew up in New Jersey and attended Northeastern University in Boston, where he acquired his first taste of biological research as a co-op student working in the laboratory of Peter Bernfield at Tufts University School of Medicine. From the beginning, Richard and metabolism were a match made in heaven. After graduation he moved to Brown University to complete his Ph.D. with Paul F. Fenton, working on the metabolic consequences of obesity in mice. Following a two year stint as an officer in the Army's Nutrition Laboratory in Denver, where he continued to study lipid metabolism, he returned to the east coast and the Fels Research Institute at Temple University in 1965 as a postdoctoral fellow with Sidney Weinhouse. Here he first encountered the enzyme that would fascinate him for the rest of his life—phosphoenolpyruvate carboxykinase, better known as PEPCK.

Richard's interest in the cytosolic form of PEPCK (PEPCK-C) stemmed from his broader curiosity about the metabolic flux of key carbohydrates and fatty acids during changes in dietary status. PEPCK-C is the rate-limiting step in gluconeogenesis in liver, but it is also present and tightly regulated in kidney and adipose tissue. This posed a conundrum of sorts, as neither kidney nor adipose tissue was thought to synthesize glucose. Together with his collaborators F. John Ballard, Lea Reshef, and Gilbert Leveille, Richard provided one answer by discovering a novel role for PEPCK-C in adipose tissue, in a pathway that became known as glyceroneogenesis (Ballard et al., 1967). They went on to show that this pathway is a major source of 3-glycerol phosphate for triglyceride synthesis in adipose tissue, and its misregulation has important implications for diabetes.

The levels of PEPCK-C are exquisitely regulated by diet, via the action of the hormones glucagon, insulin, and glucocorticoids. By the early 1970s, after Richard had joined the faculty at Fels, he recognized that the powerful tools of molecular biology could be used to uncover the mechanisms by which the levels of the enzyme fluctuated upon fasting and refeeding. It took courage to professionally switch gears and learn a new trade in mid-career, but that decision paid off handsomely over the years. It led to a long string of discoveries that produced an amazingly comprehensive understanding of the factors that regulate the transcription of PEPCK-C (Yang et al., 2009). Throughout this period Richard adopted any approach that would move the story forward, from transgenics to knockouts, from transcription factor acetylation to gene therapy. But there was never a question of what motivated this work—it was a passion to understand the role of PEPCK-C in metabolism. He never thought of himself as a card-carrying molecular biologist, although he practiced the art with great skill. As a lifetime devotee of metabolism, it must have given Richard enormous pleasure to witness the resurgent interest in the field over the last decade.

Richard W. Hanson

In 1978 Richard moved to Case Western Reserve School of Medicine to chair its Department of Biochemistry. The department was the home of Harland Wood and Merton F. Utter, two legendary leaders in the field of metabolic regulation, and Richard relished the idea of following in the footsteps of two of his scientific heroes. At Case, Richard soon became a legend himself, as a teacher and a university citizen. His biochemistry classes for both undergraduates and medical students regularly received rave reviews, and he was the recipient of numerous teaching awards. His prowess in the classroom was on display at Princeton in 2001–2002, where he was appointed the 250th Anniversary Distinguished Teaching Professor. In one semester he proved to my disbelieving colleagues that undergraduates could actually *enjoy* learning biochemistry! We still talk about his performance—for performance it certainly was—with something approaching awe.

What Richard was able to convey to his students was his enormous enthusiasm for discovery. He was also a "simplifier," as he described in a 2010 interview (Zagorski, 2010): "In my view, there are two types of teachers, 'simplifiers' and 'complicators.' The latter take a complicated subject and make it more complicated. I am a simplifier, always concerned about the complexities of biochemistry, but I try to make the subject clear to the students."

At Case Western Reserve, Richard continued his work on the transcriptional

control of PEPCK-C and its role in the regulation of gluconeogenesis and glyceroneogenesis. He garnered international attention in 2007 with a transgenic mouse that he and his colleague Parvin Hakimi created to overexpress PEPCK-C in skeletal muscle (Hakimi et al., 2007). To their surprise the mouse exhibited a dramatic collection of phenotypes, including extraordinary endurance during exercise, lean physique, increased fecundity, and extended lifespan. To say that this mouse caused a stir in the media—and among venture capitalists—would be a gross understatement. Of course, Richard was more interested in understanding the metabolic underpinnings of "Mighty Mouse"—a puzzle that Richard tackled with his usual gusto.

Throughout his scientific career, Richard formed productive and mutually rewarding collaborations with colleagues at home and around the world, beginning with John Ballard in Australia and Lea Reshef in Israel. In the age before electronic communications, they managed to keep in close touch, motivated by their mutual interest in metabolic regulation. As a graduate student in Richard's lab in the 1970s, I was inspired by their intellectual generosity to one another and impressed with the benefits that accrued from their very different ways of thinking about problems. As a seasoned investigator in the 1990s, I joined forces again with Lea and Richard to make tissue-specific PEPCK-C knockouts and experienced once again the great pleasure of planning and executing experiments with them.

Richard was immensely loyal to his collaborators and his students, as well as to institutions that mattered to him. He was a devoted contributor to the *Journal of Biological Chemistry*, publishing regularly in its pages, and serving on its editorial board and as Associate Editor for over 25 years. He was an active member of the American Society of Biochemistry and Molecular Biology, and served as its President in 1999. His commitment to service extended to his home institution, where he was greatly admired as a university citizen and—quite simply—beloved by all. In recognition of his many contributions to scholarship, teaching, and service, he was awarded the Frank and Dorothy Humel Hovorka Prize in 2001, the single highest honor that Case Western Reserve bestows on a faculty member, and named an inaugural Distinguished University Professor in 2010. As prestigious as those honors are, I suspect that Richard was just as pleased with the award he received from his students for his commitment to their education, and from his women faculty colleagues who awarded him the Gender Equity Award.

Richard's distinguished career was honored with many external awards as well, including the William C. Rose and ASBMB/Merck awards from the ASBMB, the Mead John and Osborne/Mendel awards from the American Institute of Nutrition, the Maurice Saltzman Award from the Mt. Sinai Health Care Foundation, and the Lifetime Achievement in Diabetes Research Award. He was elected to the Institute of Medicine in 1987.

In the 2010 interview, Richard said, "When I began my career in science, I thought that the most important thing that I would do was research, but as I grow older, I realize that the greatest contribution that anyone can make in our society is to be a positive influence on the lives of those you teach" (Zagorski, 2010). Those of us who were privileged to know this man and learn from him will be forever grateful.

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REFERENCES

Ballard, F.J., Hanson, R.W., and Leveille, G.A. (1967). J. Biol. Chem. *242*, 2746–2750.

Hakimi, P., Yang, J., Casadesus, G., Massillon, D., Tolentino-Silva, F., Nye, C.K., Cabrera, M.E., Hagen, D.R., Utter, C.B., Baghdy, Y., et al. (2007). J. Biol. Chem. *282*, 32844–32855.

Yang, J., Reshef, L., Cassuto, H., Aleman, G., and Hanson, R.W. (2009). J. Biol. Chem. *284*, 27031–27035.

Zagorski, N. (2010). ASBMB Today, September 2010 Issue. http://www.asbmb.org/asbmbtoday/asbmbtoday_article.aspx?id=9170.